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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/867,958	05/29/2001	Henry Yue	PC-0041 CIP	2217

27904 7590 09/24/2003

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EXAMINER
HAMUD, FOZIA M

ART UNIT	PAPER NUMBER
1647	14

DATE MAILED: 09/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

FILE COPY

Office Action Summary	Application No.	Applicant(s)	
	09/867,958	YUE ET AL.	
	Examiner	Art Unit	
	Fozia M Hamud	1647	

-- The MAILING DATE of this communication app ars on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 June 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disp sition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *7-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Receipt of Applicants' arguments and amendment, filed on 30 June 2003 in Paper No.13, is acknowledged. Claims 1 and 2 have been amended. Claims 1-20 are pending. Claims 1-6 are under consideration. Claims 7-20 stand withdrawn from prosecution as being drawn to a non-elected invention.

2. The following previous objection is withdrawn in light of Applicants amendments filed in Paper No.13, 06/30/03:

(I) The objection to the title is withdrawn.

(II) The objection to claim 2, for reciting non-elected SEQ ID Nos is withdrawn.

(III) The rejection of claims 1-6 made under 35 U.S.C. 101. The data provided in Example VIII, page 34, lines 30-35, is sufficient to provide a specific and substantial asserted utility or a well established utility, for the cDNA claimed in instant claim 2. Specifically, the disclosure that the cDNA of SEQ ID NO:2 is expressed in uterus tumor leiomyoma and not in normal myometrial tissues or in endometriosis, provides specific utility for the nucleic acid of SEQ ID NO:2 in using to diagnose uterus tumor leiomyoma.

Response to Applicants' Arguments and Amendment:

3. ***Priority:***

Applicants argue that there is no need for the Office to make a determination as to whether the requirement of 35 U.S.C. 120, that an earlier nonprovisional application discloses the invention of the second application in the manner provided by the first paragraph 35 U.S.C. 112, is met, unless in the case of an interference or to overcome a reference. Applicants submit that the instant application is properly identified as a

continuation-in-part of USSN 09/325,993 and 08/948,1997 and contains substantial portion of all of these priority applications. Applicants further argue that the Examiner has not provided any evidence that earlier nonprovisional applications (i.e 09/325,993) does not disclose the invention of the instant application in the manner provided by the first paragraph of 35 U.S.C. 112.

These arguments have been considered but are deemed unpersuasive. Firstly, in order for Applicants to overcome the rejection of claims 1-6 made under 35 U.S.C. 102(b) as being anticipated by Yue et al (WO 99/19483 issued on 22 April 1999), the Office must determine whether the invention claimed in the instant application is supported by the parent applications in a manner that fulfills the requirements, under 35 U.S.C. 112, first paragraph, (i.e, how to make and use the claimed invention). Secondly, the Examiner does not dispute that the instant application is properly identified as a continuation-in-part of USSN 09/325,993 and 08/948,197 and that it contains substantial portion of all of the priority applications, however, the Examiner's position is that, although the claimed nucleic acid sequence and the encoded polypeptide are disclosed in USSN 09/325,993 and 08/948,197, neither of the parent applications provide a specific and substantial asserted utility or a well established utility for the instantly claimed sequences. Therefore, the parent applications have not satisfied the requirements of 35 U.S.C. 112, first paragraph, regarding as to how to use the claimed invention. Accordingly, the subject matter defined in claims 1-6 is afforded an effective filing date of 29 May 2001, which is the filing date of the current application. The parent applications disclose that northern analysis shows the expression of this

sequence in various libraries, at least 67% of which are immortalized or cancerous and at least 33% of which involve immune response, and that the protein of the instant invention is also expressed in neurological, respiratory, female reproductive, gastrointestinal and hematopoietic/immune tissues, (page 14 of 09/325,993, lines 10-14). However, neither application provides any evidence that the claimed sequence is actually expressed only in cancerous tissues and not in normal tissues. Example VIII, on page 33, line 21 to page 35 line 1 of the instant specification is not found in either of the parent applications. This Example discloses that the nucleic acid of SEQ ID NO:2 is expressed in uterus tumor leiomyoma and not in normal myometrial tissues or in endometriosis. In conclusions, since the parent applications do not teach how to use the claimed invention in a manner that satisfies the requirements, under 35 U.S.C. 112, first paragraph, the claimed invention is not afforded the filing date of any of the parent applications. Accordingly, instant claims 1-6 are accorded the filing date of the instant application, which is 29 May 2001.

Claim Rejections - 35 U.S.C. § 112:

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> **The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.**

4a. Claims 1, 3-6 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

Claim 1 of the instant Application is drawn to an isolated nucleic acid encoding the polypeptide of SEQ ID NO:1 or which encodes variants of SEQ ID NO:1, or which encodes a protein having 95% sequence identity to the protein of SEQ ID NO:1. The written description in this case is only commensurate to an isolated nucleic acid encoding the polypeptide of SEQ ID NO:1, and therefore the written description is not commensurate in scope with the claims drawn to nucleic acid encoding variants of the polypeptide of SEQ ID NO:1. Adequate written description requires more than a mere statement that it is part of the invention.

To satisfy the written description requirement, an applicant's specification must reasonably convey to those skilled in the art that the applicant was in possession of the claimed invention as of the date of invention. Furthermore, the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. Adequate written description requires more than a mere statement that it is part of the invention. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. In the instant case, Applicants are claiming nucleic acids which encode variants of the polypeptide of SEQ ID NO:1, however, Applicants have not described the structure of said nucleic acids.

Support for variants is provided in the specification on page 9, lines 4-10, wherein it is disclosed that "variant" refers to molecules that are recognized as

variations of a cDNA or a protein encoded by the cDNA, which includes splice variants and allelic variants. However, no disclosure, beyond the mere mention of variants is made in the specification. This is insufficient to support the generic claims as provided by the Interim Written Description Guidelines published in the Federal Register at Volume 64, at 64 FR 71427, on 21 December 1999, and in the official gazette at 1231 O.G. 123, on 29 February 2000. The skilled artisan can not visualize the structure of all the nucleic acids encompassed by the claims.

Therefore, it does not appear that the inventors were in possession of isolated nucleic acid encoding variants of SEQ ID NO:1, or which encodes a protein having 95% sequence identity to the protein of SEQ ID NO:1.

4b. Claims 1, 3-6 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid consisting the nucleotide sequence set forth in SEQ ID NO:2, and an isolated nucleic acid comprising a nucleotide sequence which completely hybridizes to the nucleotide sequence set forth in SEQ ID NO:2, does not reasonably provide enablement for an isolated nucleic acid encoding the polypeptide of SEQ ID NO:1 or which encodes variants of SEQ ID NO:1, or which encodes a protein having 95% sequence identity to the protein of SEQ ID NO:1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Instant claims 1, 3-6 are drawn to nucleic acid encoding a protein having the amino acid sequence set forth in SEQ ID NO:1 or encoding a variant of the amino acid

of SEQ ID NO:1, or encoding a protein having 95% to the polypeptide of SEQ ID NO:1, a vector comprising said nucleic acid, a host cell comprising said vector and a method of using said nucleic acid to produce the encoded protein. However, instant specification does not teach how to use the nucleic acid claimed in instant claims 1, 3-6. Instant specification provides data showing the expression of the nucleic acid of SEQ ID NO:2 in uterus tumor leiomyoma and not in normal myometrial tissues or in endometriosis, (see Example VIII). Therefore, the skilled artisan would be able to use the nucleic acid of SEQ ID NO:2 to diagnose uterus tumor leiomyoma. However, instant specification fails to provide guidance as to how to use all possible nucleic acids encoding a protein having the amino acid sequence set forth in SEQ ID NO:1 or encoding a variant or encoding a protein having 95% to the polypeptide of SEQ ID NO:1, as claimed in claims 1, 3-6.

In their response to the office action mailed on 04 April 2003, Applicants contend that the claimed nucleic acid corresponds to a gene that is expressed in human tissue, in particular in uterine tumor tissue and can be used to diagnose certain cancers, such as squamous cell carcinoma of the lung and esophagus and uterine leiymyoma. For support of this last arguments, Applicants point to Example VIII, which details the specific expression of SEQ ID NO:2 in neoplastic disorders, particularly squamous cell carcinoma of the lung and esophagus and uterine leiymyoma. Applicants also assert that the claimed nucleic acid encodes a protein that is a member of the class of molecular co-chaperone, whose biological function are to mediate the chaperone functions of heat-shock proteins such as Hsp90. Applicants also argue that they do not

agree with the Examiner's allegation that the biological function or role of the human p23 is not understood.

Applicants' arguments have been fully considered but are not found persuasive. With respect to Applicants' first argument, while the full length nucleic acid of SEQ ID NO:2 can be used to diagnose uterus tumor leiomyoma, it is can not be used to diagnose squamous cell carcinoma of the lung or esophagus, because firstly, it is unclear from Example VIII of the instant specification as to the nature of the lung tissues used for the studies. For example, LUNGNOT28 which has a high expression of SEQ ID NO:2 is described as being a cytologically normal but obviously affected lung tissue. The specification also states that SEQ ID NO:2 was not expressed in lung tissue of normal subjects, or subjects diagnosed with asthma or in other kinds of cancerous lung tissue libraries, (see page 34, lines 10-20). Therefore, it is unclear what type of cancer is LUNGNOT28 tissue and how many libraries of this tissue is used, to establish whether said expression is statistically significant. With respect to using the claimed nucleic acid to diagnose squamous cell carcinoma of the esophagus, instant specification discloses the expression of the nucleic acid of SEQ ID NO:1 in one single library of squamous cell carcinoma of the esophagus library compared to three normal libraries. Thus this is not statistically significant data to establish that the nucleic acid of SEQ ID NO:2 is only expressed in squamous cell carcinoma of the esophagus.

With respect to Applicants' argument that he claimed nucleic acid encodes a member of a class of molecular co-chaperones, instant specification does not establish that the claimed nucleic acid encodes a protein that is a member of the class of

molecular co-chap3rones. The specification only discloses that the PR23P of the instant invention shares specific chemical and structural properties, in particular of the aspartic acid rich, C-terminus and similar isoelectirc points and that it shares 39% identity with human p23. However, all proteins that have an aspartic rich C-terminus or similar isoelectirc points do not have a common utility. With respect to Applicants' last argument, the Examiner's stands corrected and agrees with Applicants that the biological function and role of the human p23 is well understood. However, this does not mean that the biological function and role of the PR23P of the instant invention is also well understood, since Applicants have not provided any evidence that it functions as a co-chaperone.

Therefore, only the nucleic acid of SEQ ID NO:2 (full length) and an isolated nucleic acid comprising a nucleotide sequence which completely hybridizes to the nucleotide sequence set forth in SEQ ID NO:2, can be used for diagnostic purposes, i.e, to diagnose uterus tumor leiomyoma. However, neither nucleic acid encoding the protein of SEQ ID NO:1 nor a nucleic acid encoding a variant of SEQ ID NO:1 or one that is encodes a protein having 95% identity to SQE ID NO:1, nor the encoded protein itself can not be for diagnostic purposes. Applicants have not shown that any other nucleic acid or variant, even degenerate variants encoding the same protein was expressed in uterus tumor leiomyoma. Thus, while the nucleic acid comprising the nucleotide sequence set forth in SEQ ID NO:2, (full length) may be used to detect uterus tumor leiomyoma, due to increased copy number, the increased copy number of SEQ ID NO:2 does not provide a readily apparent use for all nucleic acids comprising

the nucleotide sequences encoding the polypeptide of SEQ ID NO:1, or those that encode variants of SEQ ID NO:1 because there is no information regarding whether degenerate variants encoding the same protein, were increased in uterus tumor leiomyoma compared to normal controls.

The data in the instant specification shows that gene copy number is increased in certain tumor tissue samples, however, it does not necessarily follow that an increase in gene copy number results in increased gene expression and increased protein expression, such that "all possible" nucleic acids encoding the polypeptide of SEQ ID NO:1, or those that encode variants of the polypeptide of SEQ ID NO:1, would be useful diagnostically or as target for cancer drug development. For example, Pennica et al, (1998, PNAS USA 95:14717-14722) discloses that, "An analysis of WISP-1 gene amplification in human colon tumors showed a correlation between DNA amplification and over expression, whereas, over expression of WISP-3 RNA was seen in the absence of DNA amplification. In contract, WISP-2 DNA was amplified in the colon tumors, but mRNA expression was significantly reduced in the majority of tumors compared with the expression in normal colonic mucosa from the same patient", see page 14722, second paragraph of column 1; pages 14720-14721. Therefore, the protein levels cannot be accurately predicted from the level of the corresponding gene.

Thus, while instant specification is enabling for an isolated nucleic acid comprising the nucleotide sequence set forth in SEQ ID NO:2, the specification is non enabling for an isolated nucleic acid encoding the polypeptide of SEQ ID NO:1 or an isolated nucleic acid encoding variants of the polypeptide of SEQ ID NO:1.

Claim Rejections - 35 U.S.C. §102:

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5a. Claims 1-6 stand rejected under 35 U.S.C. 102(b) as being anticipated by Yue et al (WO 99/19483 issued on 22 April 1999), for reasons of record, set forth in the office action mailed on 04 April 2003 in Paper No:12, pages 5-6, and reiterated here.

Applicants argue that the claimed invention as recited in claims 1-6, is fully entitled to the effective filing date of priority application 09/948,197, filed on 9 October 1997, therefore, Yue et al does not anticipate SEQ ID NO:1 or SEQ ID NO:2.

This argument is not found persuasive, because the invention of instant claims 1-6 is not entitled for the effective filing date of the priority application 09/948,197, filed on 9 October 1997, nor is it entitled for the effective filing date of the priority application 09325,993, filed on 04 June 1999, but is rather entitled to the filing date of the instant application, 9 May 2001, because neither of the parent applications teaches how to use the claimed invention in a manner that satisfies the requirements, under 35 U.S.C. 112, first paragraph. See paragraph 3 of this office action.

Conclusion:

6. No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Advisory Information:

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fozia M Hamud whose telephone number is (703) 308-8891. The examiner can normally be reached on Monday, Wednesday-Thursday, 6:30 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (703) 308-4623. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Fozia Hamud
Patent Examiner
Art Unit 1647
27 August 2003

YVONNE EYLER, PH.D
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